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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,169	10/21/2003	R. Kent Hermsmeyer	HME/7961.0013	3934

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,169	HERMSMEYER, R. KENT	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restrictions

Applicant's election of group I, claims 1-16 in the reply filed on 12/18/2006 is acknowledged. Claims 17-23 are withdrawn from consideration. The examiner thanks the applicant for pointing out the mistake of incorrectly stating to elect the species from claim 11 instead of claim 12 upon election of group I. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Thus the restriction requirement elected is made final. Claims 1-16 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Anthony (Am. Soc. For Nutritional Sciences J Nutr. 130, 662S-663S, 2000).

Anthony teaches that genistein, an estrogen beta receptor agonist inhibited serotonin uptake in platelets further teaches that isoflavones might inhibit platelet activation and aggregation and reduce the amount of serotonin in the platelets, all of which could contribute to a reduction in coronary vasospasm and thrombosis (P 663S, lines 21-28).

Claims 1-3 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (J Neurosurg 89, 289-296, 1998).

Kim et al. teaches that genistein (30 and 100 μM) reduced markedly the contraction of rabbit basilar arteries induced by erythrocyte lysate (p 293, col. 2, lines 3-4). The reference teaches that coronary vasospasm, a persistent narrowing of major cerebral arteries is followed by subarachnoid hemorrhage (p 289, lines 1-4). The reference further teaches that genistein exerts a stronger inhibitory action over receptor activation induced contraction in peripheral vascular tissues (p 294, lines 17-20).

Claims 1-3, 8,15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Honore et al. (Fertility and sterility, 67, 1, 1997).

Honore et al. teaches that administration of genistein (IV infusion), an estrogen receptor agonist enhanced coronary vasodilation in female monkeys. The reference further teaches the long term oral consumption of soy isoflavones (diet) that includes genistein and short-term administration of genistein in female monkeys changed the constrictor response to dilation (characteristic of normal primate coronary arteries) (P149, col.1, lines 5-42, p152, col.1, lines 12-24).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony (Am. Soc. For Nutritional Sciences J Nutr. 130, 662S-663S, 2000) in view of Weihua et al. (PNAS, 2002, 99, 13589-94).

Anthony's teachings discussed as above. The reference does not teach the 5α-androstane-3β,17 β-diol or any of the derivatives in reducing the incidence or severity of vascular hyperreactivity.

Weihua et al. teaches 5α-androstane-3β,17 β-diol to be an estrogen receptor beta agonist ligand (see Abstract).

Claims 5 and 6 are rejected based on close structural similarity of the derivatives with 5α-androstane-3β,17 β-diol. It is obvious that compounds with very close structural similarities will have similar utilities and hence the derivatives of 5α-androstane-3β,17 β-diol will function as estrogen beta-receptor agonists.

The examiner would like to point out that a prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (discussed in more detail below) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).

It would have been obvious to one of ordinary skill in the art at the time of invention to administer 5α-androstane-3β,17 β-diol and its derivatives for genistein. The

motivation to do so is by administering one estrogen receptor beta agonist for another would provide similar or superior efficacy in the therapeutic treatment of vascular hyperreactivity.

Claims 1, 9,10, 13, 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony (Am. Soc. For Nutritional Sciences J Nutr. 130, 662S-663S, 2000) in view of Weihua et al. (PNAS, 2002, 99, 13589-94) and further in view of Fujikawa et al. (J of Cerebral Flow and Metabolism, 1999, 19, 44-52).

The teachings of Anthony and Weihua et al. have been discussed in the 103(a) rejection set forth above.

Anthony and Weihua et al. do not teach the amount of administration of estrogen beta-receptor agonist in the treatment of vascular hyperreactivity.

Fujikawa et al. teaches the reversal of vasospasm by genistein by topical application of genistein to the spastic basilar artery (1×10^{-6} to 3×10^{-4} mol/L genistein; 270 pg/ml – 810×10^{2} pg/ml).

It would have been obvious to one of ordinary skill in the art at the time of invention to administer an estrogen beta receptor agonist such as 5α-androstane-3β,17 β-diol in an sufficient amount to obtain 30-3000 pg/ml in serum because Fujikawa et al. teaches that administration of 1×10^{-6} to 3×10^{-4} mol/L (270- 810 pg/ml) genistein, an estrogen beta receptor agonist reverses vasospasm.

Claims 1, 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony (Am. Soc. For Nutritional Sciences J Nutr. 130, 662S-663S, 2000) in view of Barkheim et al. (Molecular Pharmacology, 54, 105-112, 1998).

Anthony's teachings discussed as above. The reference does not teach the epiestriol in reducing the incidence or severity of vascular hyperreactivity.

Barkheim et al. teaches that epiestriol has an ER-beta selective agonist potency.

It would have been obvious to one of ordinary skill in the art at the time of invention to administer epiestriol for genistein. The motivation to do so is by administering one estrogen receptor beta agonist for another would provide similar or superior efficacy in the therapeutic treatment of vascular hyperreactivity.

Claims 1, 11,12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Honore et al. (Fertility and sterility, 67, 1, 1997).

Honore et al. does not teach the co-administration of estrogen beta-receptor agonist with a hormone replacement therapy.

The reference teaches that atherosclerosis impairs endothelium-mediated coronary artery dilation in male and postmenopausal female human and non human primates which may play role in vasospasm, angina and myocardial infarction and one of the mechanisms by which estrogen replacement therapy may reduce the risk of coronary vascular reactivity among postmenopausal women is by improving the coronary vascular reactivity (p145, col.1 lines 15-22). The reference teaches that postmenopausal estrogen replacement therapy is conjugated with estrogens given orally with or without progestin (p 148, col.1, col. 2, lines 1-6). The reference further teaches that genistein, an estrogen beta-receptor agonist enhanced coronary vasodilation in female monkeys (p 152, lines 15-18).

It would have been obvious to one of ordinary skill in the art at the time of invention to use an estrogen beta-receptor agonist along with an hormone such as progestin in a method of reducing the incidence or severity of vascular hyperreactivity. The motivation to do is taught by Honore et al. The reference teaches that estrogen replacement therapy may reduce the risk of coronary vascular reactivity among postmenopausal women by improving the coronary vascular reactivity. The reference further teaches that genistein, an estrogen beta-receptor agonist enhanced coronary vasodilation in female monkeys. Hence it would have been obvious to one of ordinary skill in the art to combine compounds that are useful in reducing the risk of coronary vascular reactivity to provide synergistic effects.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER